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LETTERS AND CORRESPONDENCE

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Lymphadenopathy Associated With Monoamine Oxidase Inhibitors

To the Editor: Non-neoplastic lymphadenopathy remains in the differential diagnosis in patients who present with generalized lymph node enlargement. Certain medications are known to cause hypersensitivity reactions with associated lymphadenopathy in susceptible individuals [1–3]. (Table I). The classic drug associated with adenopathy is the hydantoin derivative, phenytoin [4]. Typically, adenopathy occurring in the cervical lymph nodes reveal on biopsy nonspecific features similar to viral-induced lymphadenopathy. Making the correct diagnosis in this situation is critical in a treatment decision. We report a patient whose drug-associated lymphadenopathy required multiple biopsies and extensive surgery. This is the first report of lymphadenopathy caused by monoamine oxidase inhibitors (MAOI).

A 54-year-old male with a history of depressive disorder being treated with phenelzine (Nardil®) for 20 years sought medical attention in 1992 for cervical lymphadenopathy. The patient had multiple lymph nodes in the neck, the largest measuring 5 × 4 cm, and a right supraclavicular mass measuring 3 × 3 cm. The spleen was normal. Computerized tomography (CT) of the chest, abdomen, and pelvis revealed only the presence of peritracheal adenopathy. Biopsy of the right supraclavicular mass was consistent with lymphoid hyperplasia. Serology for Epstein-Barr virus (EBV), human immunodeficiency virus (HIV), cytomegalovirus (CMV), and toxoplasmosis were negative. Pan endoscopy of the oral cavity and upper airway did not reveal any malignancies. Progressive adenopathy resulted in a right radical neck dissection with the pathological diagnosis of lymphoid hyperplasia. One year later, new adenopathy appeared in the base of the neck and right axilla. Biopsy of the latter revealed the same diagnosis. Restaging with CT scan showed no evidence of other lymphadenopathy. At this time, phenelzine was discontinued and buproprion (Wellbutrin®) was initiated. Four months after discontinuation of the phenelzine, the lymphadenopathy decreased in size, then resolved completely two months later. Tranylcypromine (Parnate®), another MAOI was substituted for buproprion because of poor psychiatric response. Three months later, the patient sought medical attention for reappearance of cervical and supraclavicular adenopathy. Currently the patient is unwilling to discontinue tranylcypromine because of its efficacy as an antidepressant.

TABLE I. Drugs Associated With Lymphadenopathy*

Phenytoin	Carbamazepine
Para-amino salicylic acid	Phenylbutazone
Indomethacin	Aspirin
Sulfonamides	Iron-Dextran
Pencicillins	Erythromycin
Gentamicin	Tetracycline
Thiouracil compounds	Sulfasalazine
Griseofulvin	Anti-thymocyte globulin
OKT-3	Gold
Halothane	Bacille Calmette-Guerin
Allopourinol	Insulin
Primidone	Methyldopa, Levopdopa

*From Segal G, Clough JD, Tubbs RR. Autoimmune and iatrogenic causes of lymphadenopathy. Semin Oncol 1993;20:611.

To our knowledge, MAOI have not been associated with drugs causing lymphadenopathy. Our patient experienced lymphadenopathy years after being treated with an MAOI. Three lymph node biopsies revealed lymphoid hyperplasia. After withdrawal of the latter, his lymphadenopathy disappeared only to reoccur upon rechallenge with a second MAOI, tranylcypromine. Recognition of the nonneoplastic nature of drug induced lymphadenopathies continues to be an important aspect of clinical management. Clinicians should be aware of the possible occurrence of lymphadenopathy with this class of antidepressants.

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REFERENCES

1. Segal G, Clough JD, Tubbs RR. Autoimmune and iatrogenic causes of lymphadenopathy. Semin Oncol 1993;20:611–626.
2. Yates P, Stockdill G, McIntyre M. Hypersensitivity to carbamazepine presenting as pseudolymphoma. J Clin Pathol 1986;39:1224–1228.
3. Rothschild B, Marshall H. Lymphadenopathy and lymph node infarction in the course of gold therapy. Am J Med 1986;80:537–540.
4. Abratt RP, Sealy R, Uys CJ, Lawson R. Lymphadenopathy associated with diphenylhydantoin therapy. Clin Oncol 1982;8:351–354.

Fulminant Brain Lymphoid Infiltration in a Patient With Chronic Lymphocytic Leukemia

To the Editor: Symptomatic involvement of the central nervous system (CNS) in chronic lymphocytic leukemia (CLL) is very rare. We present a

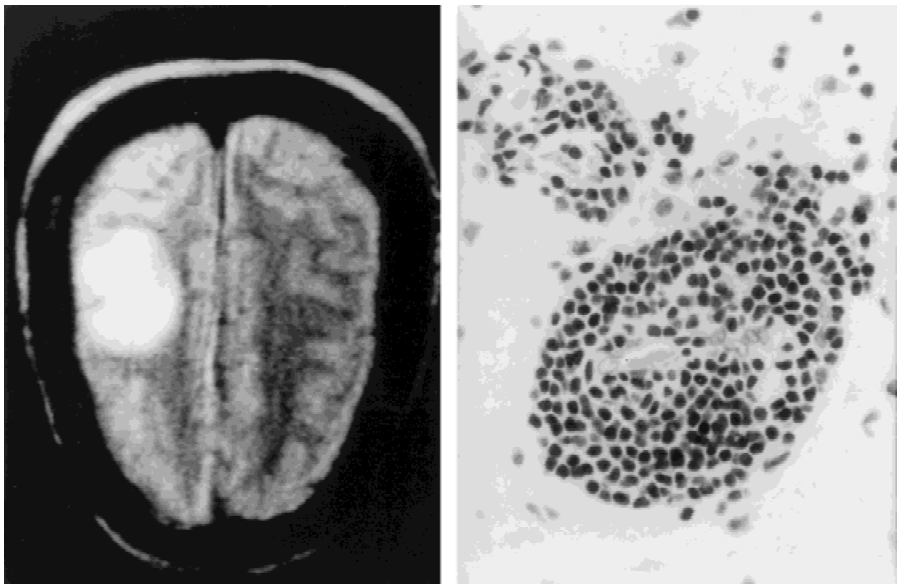

Fig. 1. Left: MRI of brain with T2 showing a hyperintense lesion in left fronto-parietal subcortical area. Right: Perivascular lymphocytic infiltrate.

patient with leukemic infiltration of the CNS shown on cerebral biopsy. We underline the complexity of diagnosis and the need to suspect this complication when there are neurological clinical signs.

A 60-year-old gypsy woman presented with B type CLL, Rai stage 0. Thirty-four months after the diagnosis she required treatment (chlorambucil 30 mg/m^2/monthly) for the appearance of bilateral axillary lymphadenopathies and duplication of the leukocyte count. Sixty-six months after commencing treatment, the patient had difficulty speaking and deviation of the oral commissure. On examination, the patient was conscious and orientated, had right central facial paralysis and slurred speech. Osteotendinous reflexes were normal. Babinski's sign was negative. Electromyogram, electrocardiogram, and carotid ecodoppler were normal. Cranial computed tomography (CT) showed a hypodense left parieto-occipital subcortical area that was not changed on intravenous contrast. Because an ischemic lesion was suspected, antiaggregate treatment was started. In view of the unfavorable course, with motor aphasia and right hemiparesia with a positive right Babinski's sign, magnetic resonance imaging scan (MRI) was done which showed a hypodense area in T1 and hyperintense in T2 (this lesion was not affected by gadolinium). A space-occupying lesion was seen and cerebral biopsy showed a perivascular lymphoid infiltrate compatible with CLL (Fig. 1). Cranial radiotherapy was not tolerated because of convulsions, and a cycle of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy was given, to no avail. The patient's condition worsened rapidly. She became unconscious, comatose, and died 50 days after the onset of symptoms.

Symptomatic lymphoid infiltration of the CNS is rare. However, asymptomatic CNS infiltration has been shown at autopsy in between 8% and 70% of cases depending on the series [1,2]. The mechanism of invasion of the CNS by the CLL lymphocytes is unknown. The morbid anatomy in these cases is varied. Our patient had perivascular infiltration of CLL lymphocytes. However, other forms of presentation are leukemic meningitits, or lymphocytes extravasated by bleeding [3]. Diagnosis is difficult because of the varied clinical picture. A differential diagnosis of neurological signs includes infectious, vascular and infiltrating conditions, degenerative and demyelinating disorders. In our case, brain parenchymal involvement was suggested by CT but this lesion was detected by MRI and confirmed by the histology. Study of the cerebrospinal fluid (CSF) may be confusing because it is difficult to distinguish between the CLL lymphocytes and the normal lymphocytes present during viral infections. CSF immunohistochemistry is important. Depending on the patient's clinical condition, cerebral biopsy may not be possible. Consequently, when brain involvement is suspected and in view of the aggressivity of the presentation of such conditions, early diagnosis by imaging techniques is extremely important in order to start treatment as soon as possible [4,5]. We would like to emphasize the fact that CLL may involve the CNS without preceding meningeal spread and may be present at all stages of CLL [1].

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References

1. Cramer SC, Glaspy JA, Efird JT, Louis DN. Chronic lymphocytic leukemia and the central nervous system: a clinical and pathological study. Neurology 1996;46: 19–25.
2. James HB, Hammack JE, McDonnell SK, Tefferi A. The neurologic complications of B-cell chronic lymphocytic leukemia. Neurology 1997;48:407–412.
3. Azzarelli B, Roessmann U. Pathogenesis of central nervous system infiltration in acute leukemia. Arch Pathol Lab Med 1997;101:203–205.
4. Quitt M, Bazac I, Gross B, Aghai E. Fulminant bilateral cerebellar syndrome in a patient with chronic lymphocytic leukemia. Leuk Lymphoma 1994;15:507–510.
5. Pohar S, deMetz C, Poppema S, Hugh J. Chronic lymphocytic leukemia with CNS involvement. J Neuro-Oncol 1993;16:35–37.

Successful Treatment for Acute Lymphoblastic Leukemia Without Blood Transfusion in a Jehovah's Witness

To the Editor: Intensive chemotherapy for acute leukemia usually does not achieve a high remission rate and prolonged survival without supportive

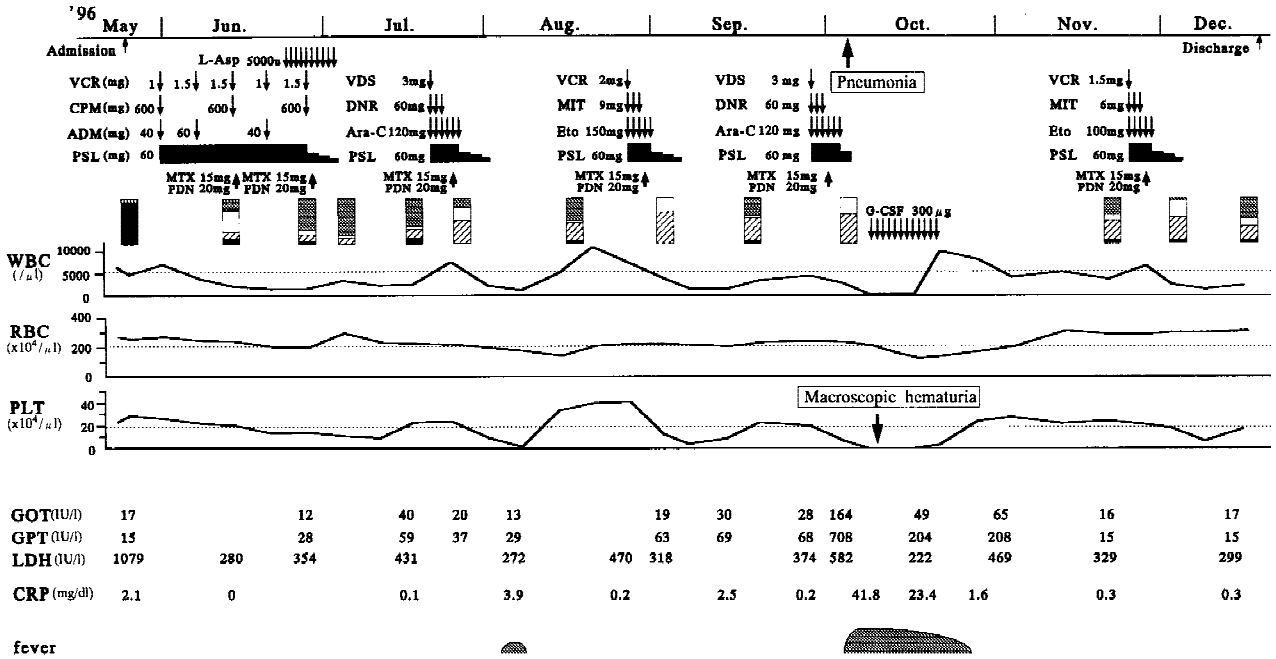

Fig. 1. Clinical course of the patient.

therapy, especially blood component transfusion. In Jehovah's Witnesses with acute leukemia, it is difficult to obtain remission because they refuse blood transfusions for religious reasons. Herein, we report a Jehovah's Witness with acute lymphoblastic leukemia (ALL) who was successfully treated by combination chemotherapy without any blood support.

A 43-year-old Japanese woman with anemia was admitted to our hospital on May 24, 1996. Physical examination revealed neither hepatosplenomegaly nor lymphadenopathy. Her hemoglobin level was 8.0 g/dl, her platelet count (Plt) was 284×10^9/L, and her white blood cell (WBC) count was 4.7×10^9/L with 35% blast cells. A bone marrow examination revealed 88% blasts. These cells stained negative for peroxidase. The surface phenotypes of the blasts in bone marrow were as follows: CD10 49.0%, CD13 0.7%, CD19 74.5%, CD33 56.6%, CD34 70.5%, and HLA-DR 82.5%. Lactate dehydrogenase level in the blood was 1,079 IU/L. Based on these findings, we diagnosed her condition as ALL.

We were notified that she was a Jehovah's Witness after she was admitted. We informed the patient and her husband about the risks of intensive chemotherapy for ALL without blood transfusion, but she refused to receive any blood component transfusion. A partial remission was achieved with remission induction therapy composed of vincristine, cyclophosphamide, adriamycin, prednisolone (PSL), and 1-asparaginase combined with intrathecal injection of methotrexate and PSL. Then, intensive consolidation chemotherapy composed of vindesine, daunorubicin, cytosine arabinoside, and PSL was initiated. After that, the patient developed liver dysfunction (grade 3 according to the Eastern Cooperative Oncology Group adverse-effect classification [1]), bronchopneumonia, and macroscopic hematuria due to leukopenia and thrombocytopenia (nadir WBC $<0.1 \times 10^9$/L, Plt 1.0×10^9/L). Therapy with antibiotics, granulocyte-colony stimulating factor without human serum albumin, and inhalated amphotericin B gave good results and bronchopneumonia and macroscopic hematuria disappeared as Plt increased. Then, liver dysfunction also improved gradually and complete remission (CR) was achieved without any blood transfusional support. Remission continued for two years but leukemic relapse occurred. The patient is now receiving reinduction chemotherapy.

Recently, Cullis et al. [2] reported one patient with ALL out of five Jehovah's Witness with acute leukemia who obtained CR without transfusion support, whereas two patients who refused to be transfused died of severe anemia shortly after the start of chemotherapy. These authors also reviewed case reports of Jehovah's Witnesses with acute leukemia and described seven patients (four ALL, three AML) who obtained CR without transfusion [2]. In general, remission of ALL may be achieved in younger patients and those without severe bone marrow aplasia [2–5]. Our patient was middle-aged and presented severe macroscopic hematuria but, fortunately, she did not have life-threatening bleeding due to severe thrombocytopenia such as cerebral, pulmonary, or gastrointestinal bleeding. Our experience also suggests that patients who refuse blood transfusion should not be excluded from receiving high-dose chemotherapy for ALL.

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References

1. Okem MM, Creach RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982;5:649–655.
2. Cullis Jo, Duncombe AS, Dudley JM, Lumley HS, Apperley JF, Smith AG. Acute leukemia in Jehovah's Witness. Br J Heamatol 1998;100:664–668.
3. Boggs DR. Jehovah's Witness with leukemia. Hosp Pract 1985;20:92–98.
4. Blutters-Sawatzki R, Bertram U. Introduction of erythropoietin in the treatment of acute lymphoblastic leukemia in a patient of Jehovah's Witness persuasion: A case report. Med Pediatr Oncol Suppl 1992;2:23–25.
5. Nousiainen T, Jantunen E, Lahtinen R. Jehovah's Witness with acute leukemia [letter]. Am J Hematol 1993;43:158–159.

Possible Role of Soyabean Therapy in Isolated Platelet Factor 3 (PF3) Availability Defect

To the Editor: Isolated platelet factor 3 (PF3) availability defect is a hereditary platelet function disorder characterized by mild-to-moderate bleeding from multiple sites. Its management is frustrating as no definite therapeutic modalities are available. Since PF3 is largely a phospholipid, an attempt was made in the present study to provide phospholipid from soyabean to correct the defect in patients with isolated PF3 availability defect.

Patients presenting with history of episodic bleeding since childhood with normal platelet counts and coagulation tests [1] (prothrombin time, activated partial thromboplastin time, clot stability) were screened for platelet function defects by bleeding time, prothrombin consumption index, PF3 availability [2], and platelet aggregation studies. Total PF3 was measured by the method of Kasturi et al. [3]. PF3 availability was measured using the method of Hardisty and Hutton [4]. Briefly, Russel viper venom time (RVVT) was performed on platelet rich plasma (PRP) at 0 min and 20 min after incubation with adenosine 5′-diphosphate (ADP). PF3 availability was considered to be reduced when the latter was greater than 19.0 sec. Patients having reduced PF3 availability, normal platelet aggregation, and PF3 content were diagnosed to have isolated PF3 availability defect [5]. Patients with renal disorders, heart disease, liver dysfunction, or medications affecting platelet functions, were excluded from the present study.

Thirty-five patients (M:F 1:2, aged between 5 and 65 years) with isolated PF3 availability defect were administered soyabean (50 gm/day) orally as boiled beans, soya flour or soya milk. A record of the frequency, site, and amount of bleeding was maintained by the patients before, during, and after soyabean therapy. Clinical response and in vitro PF3 availability was evaluated three months after soya therapy in all patients.

Complete cessation of bleeding depicting complete clinical response occurred in one patient while partial clinical response with at least 50% reduction in frequency and amount of bleeding occurred in 22 patients (Table I). No response occurred in 12 patients.

PF3 availability improved in 18 of the 35 patients with normalization in four cases and partial correction in 14 patients. No improvement in PF3 availability occurred in 17 cases, seven of whom had partial clinical response. Withdrawal of soya therapy in seven patients with clinical response resulted in increased bleeding and reinstitution of soya treatment again resulted in clinical improvement in them. Application of McNemar's paired statistical test revealed a definite positive correlation between the clinical improvement and laboratory correction of PF3 availability ($P = 0.1824225$). Eighty-six of the 87 patients with isolated PF3 availability defect who did not receive soya therapy continued to have the same severity of bleeding, whereas in one patient, clinical and laboratory correction occurred spontaneously.

Thus, soyabean therapy appears to have a beneficial effect in the management of isolated PF3 availability defect. Bleeding in this disease may be attributed to a poor configurational response of platelet membrane to ADP. Soyabean therapy probably results in availability of more phospholipid surface for the coagulation cascade to proceed, thereby resulting in clinical improvement along with correction of in vitro PF3 availability test. However, further studies are required to identify the essential component of soyabean needed to correct the underlying defect, its pharmacology, pharmacokinetics, and to elucidate its mechanism of action.

TABLE I. PF3 Availability and Clinical Response to Soya Therapy in Isolated PF3 Availability Defect

	Presence of clinical response				
PF3 availability test	Complete (CR)	Partial (PR)	Total response (CR + PR)	No clinical response	Total
Complete correction (CC)	01	03	04	00	04
Partial correction (PC)	00	12	12	02	14
Correction[a] (CC + PR)	01	15	16*	02*	18*
No correction	00	07	07*	10*	17*
Total	01	22	23*	12*	35*

[a]PF3 availability test was considered corrected completely when Russel viper venom time at 20 min was <19.0 sec and partially when it was less than the original value (by 2 sec) but more then 19.0 sec.
*McNemar's test was applied to these values ($P = 0.1824225$).

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References

1. Dacie JV, Lewis SM. Practical haematology. 8th ed. Edinburgh: Churchill Livingstone; 1994.
2. Spaet TH, Cinatron J. Studies on platelet factor 3 availability. Br J Haematol 1965;11:296.
3. Kasturi J, Saraya AK, Kishan R. A study of platelet function: primary thrombopathy. Indian J Med Res 1972;60:567–575.
4. Hardisty RM, Hutton RA. Platelet aggregation and the availability of platelet factor 3. Br J Haematol 1966;12:764–776.
5. Saraya AK, Saxena R, Dhot PS, Choudhry VP, Pati H. Platelet function disorders in North India. Natl Med J India 1994;7(1):5–7.

Acute Promyelocytic Leukemia Relapse in the Central Nervous System During Hematologic and Molecular Remission

To the Editor: Acute promyelocytic leukemia (APL) is characterized by a specific genetic abnormality, the translocation t(15;17) resulting in the formation of the PML/RARα fusion gene, and by a unique sensitivity to the differentiating agent all-*trans* retinoic acid (ATRA) [1]. Central nervous system (CNS) recurrence is rare in APL. The present case is the first report of a CNS relapse occurring after ATRA therapy in the presence of molecularly documented remission in the bone marrow (BM) of an APL patient.

A 33-year-old man was admitted to our hospital in June 1996 for asthenia and malaise. Blood counts showed: white blood cells, 54.6×10^9/l with 85% blasts and atypical promyelocytes; hemoglobin, 7.5 g/dl; and platelets 13×10^9/l. A morphologic diagnosis of AML French-American-British (FAB) M3 variant was established in BM and peripheral blood (PB). The immunophenotype was CD33+, CD13+, CD15+, HLADR−, CD14− in >80% of the cell population, while 8% of cells stained positive for CD34. Cytogenetic and molecular studies performed in BM showed the presence of t(15;17) and of bcr 2 type PML/RARα transcript. All molecular analyses were performed by hot start nested reverse-transcription polymerase chain reaction (RT-PCR) as previously described [1]. The patient was treated with the LAP/96 PETHEMA protocol, which includes simultaneous ATRA and idarubicin for induction, followed by three courses of idarubicin, VP-16 and mitoxantrone, and again idarubicin as consolidation; the doses and schedule of this protocol are the same as in the AIDA protocol [1].

The patient achieved hematologic remission after induction and con-

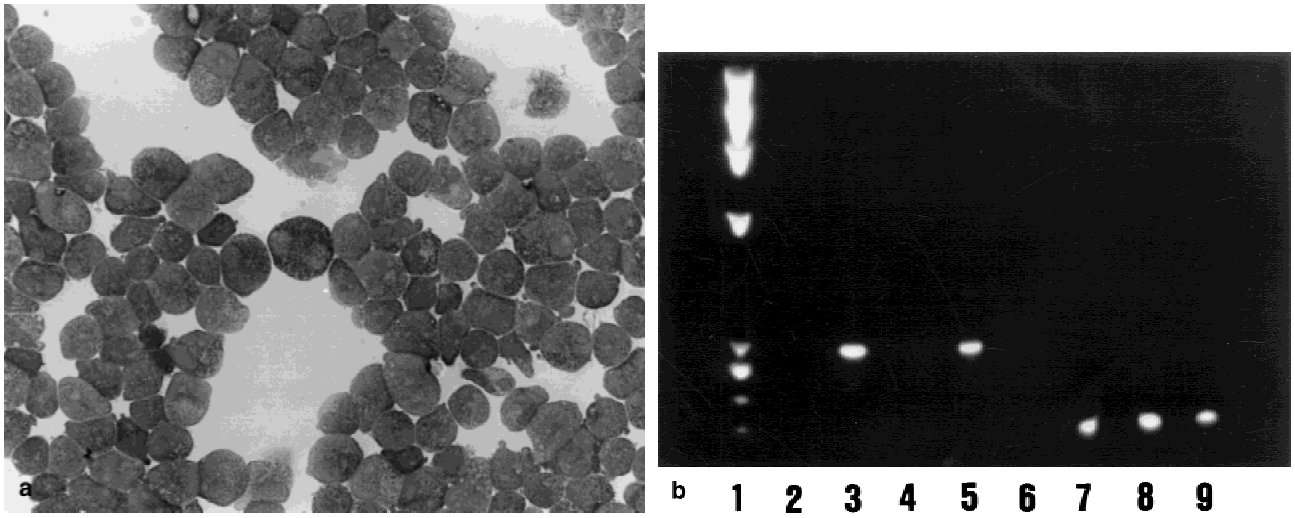

Fig. 1. a: Cerebrospinal fluid cells with APL morphologic features (Wright stain; original magnification, ×400). b: cDNA amplification of the patient described by RT-PCR for study of PML/RARα (bcr 1–2) mRNA. Line 1: Molecular weight marker (phiX174 DNA digested with Hae III). Line 2: Amplification of cDNA from bone marrow cells isolated at the time of CNS relapse, showing its negativity. Line 3: Analysis of the cells from the cerebrospinal fluid at the time of CNS relapse showing PML/RARα (bcr 2 type) positivity. Line 4: Study in BM cells of the patient described, isolated in September 1997, showing PML/RARα negativity. Line 5: Positive control (the patient described at the diagnosis, positive for bcr 2 type PML/RARα transcript). Line 6: Negative control. Line 7, 8 and 9: Amplification of non-rearranged RARα genes from the same cDNAs as line 2, 3, and 4 which were used as internal controls.

verted to PCR negative in BM after consolidation (October 1996). He therefore received maintenance therapy with intermittent ATRA and methotrexate (MTX)+6-MP, and three follow-up PCR evaluations (performed in March, June, and September 1997, respectively) showed no evidence of PML/RARα in the BM.

In October 1997, the patient came to our hospital emergency unit because of severe headache and convulsions. A lumbar puncture disclosed the presence in the cerebrospinal fluid of 960/μl cells with typical APL morphologic features (Fig. 1a). Morphologic examination of BM and PB was consistent with complete hematologic remission. The karyotype in BM was normal. PCR amplification of the PML/RARα showed the presence of the fusion gene in CNS fluid whereas BM cells tested negative (Fig. 1b). The patient received intrathecal chemotherapy with hydrocortisone, MTX, and cytosine arabinoside. In November 1997 BM was still in complete hematologic remission, and PML/RARα in BM cells was negative. Nevertheless, the disease in CNS was resistant to the intrathecal treatment.

Though infrequently, APL relapse may occur in the CNS, particularly in patients who had previously received ATRA therapy [2]. Of the cases reported after ATRA treatment, six showed hematologic or molecular evidence of disease also in BM at the time of CNS relapse [2–6], and one was not studied by RT-PCR and was in cytological remission in BM [2]. The case described here represents the first report of a CNS relapse developed after ATRA therapy in the presence of molecularly documented remission in the BM. It may be worth emphasizing that our PETHEMA regimen does not include Ara-C, the use of which allows significant pharmacologic levels to be obtained across the hematoencephalic barrier, being potentially relevant to prevent CNS disease. In the future, it will be important to define more precisely the role of ATRA and Ara-C in the pathogenesis and prevention of CNS relapse in APL.

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References

1. Mandelli F, Diverio D, Avvisati G, Luciano A, Barbui T, Bernasconi C, Broccia G, Cerri R, Falda M, Fioritoni G, Leoni F, Liso V, Petti MC, Rodeghiero F, Saglio G, Vegna ML, Visani G, Jehn U, Willemze R, Muus P, Pelicci PG, Biondi A, Lo Cocco F. Molecular remission in PML/RARα-positive promyelocytic leukemia by combined all-trans retinoic acid and idarubicin (AIDA) therapy. Blood 1997;90:1014–1021.
2. Evans G, Grimwade D, Prentice HG, Simpson N. Central nervous system relapse in acute promyelocytic leukaemia in patients treated with all-trans retinoic acid. Br J Haematol 1997;98:437–439.
3. Currie J, Chee YL, Culligan DJ. Central nervous system relapse in acute promyelocytic leukaemia treated with ATRA. Br J Haematol 1997;99:469.
4. Molero T, Valencia JM, Gómez-Casares MT. Central nervous system (CNS) infiltration in a case of promyelocytic leukemia. Haematologica 1997;82:637.
5. Wiernik PH, De Bellis R, Muxi P, Dutcher JP. Extramedullary acute promyelocytic leukemia. Cancer 1996;78:2510–2514.
6. Martino B, Vincelli I, Marino A, Comis M, Ronco F, Nobile F. Meningeal relapse in a patient with acute promyelocytic leukaemia treated with all-trans retinoic acid. Br J Haematol 1998;100:606–607.

Thrombotic Thrombocytopenic Purpura

To the Editor: We have read with great interest the recent article by Pasquale et al. [1] entitled *Chronic Relapsing Thrombotic Thrombocytopenic Purpura: Role of Therapy with Cyclosporine.*

Their patient had 18 episodes of thrombotic thrombocytopenic purpura (TTP) and had neurological symptoms such as confusion, left hemiparesis, dysarthria, and seizures.

We are wondering whether the patient has been investigated by cranial computed tomography (CT) and magnetic resonance imaging to clarify the neurologic symptoms.

Secondly, Pasquale et al. [1] stated that the highest number of TTP relapses previously described in a single patient was 11 [2]. However, their patients had 18 episodes of TTP. Several studies have revealed that most patients with recurrent thrombosis including heparin-induced thrombocytopenia and thrombosis are associated with inherited thrombophilia such as factor V Leiden mutation, protein C, S, and antithrombin III deficiencies [3,4]. It might be beneficial if they investigated the patient at least for factor V Leiden mutation.

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REFERENCES

1. Pasquale D, Vidhya R, DaSilva K, et al. Chronic relapsing thrombotic thrombocytopenic purpura: role of therapy with cyclosporine. Am J Hematol 1998;57:57–61.
2. Kitchens CS. Studies of a patient with recurring thrombotic thrombocytopenic purpura. Am J Hematol 1992;13:259–267.
3. Gardyn J, Sorkin P, Kluger Y, Kabili S, Klausner JM, Zivelin A, Eldor A. Heparin-induced thrombocytopenia and fatal thrombosis in a patient with activated protein C resistance. Am J Hematol 1995;50:292–295.
4 Gurgey A, Mesci L, Renda Y, Olcay L, Koçak N, Erdem G. Factor V 506 mutation in children with thrombosis. Am J Hematol 1996;53:37–39.